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INTENSIVE COMMUNITY OUTREACH MAY DILUTE TRANSITION TO PSYCHOSIS IN SUBJECTS AT HIGH CLINICAL RISK

Letter

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Dear Editor,

The Liaison and Education in General Practices (LEGs) cluster-randomised controlled trial¹ investigated whether increased liaison between primary and secondary care improves the detection of primary care patients at ultra-high risk (UHR) of developing psychosis or first episode-psychosis (FEP) and concluded that it was both clinically and cost effective. However, the ratio of true positives (UHR or FEP) and false positives (neither UHR nor FEP) referrals from general practices was similarly (approximately 1:1) across all the three treatment conditions (high intensity: 2.2:2.3, low intensity: 1.1:0.9, practice as usual: 0.6:0.8)¹. Thus, there is no evidence of the high-intensity intervention specifically improving diagnostic accuracy of general practitioners in UHR or FEP identification, which is the key outcome of interest. Furthermore, UHR true/false positives were defined as new referrals “who met criteria for high risk [...] according to CAARMS (psychosis true positives) and those who did not fulfill the criteria (false positives)”¹. This is problematic as, commonly, “psychosis true positive” is prognostically defined by the proportion of baseline subjects who actually transition to psychosis (i.e. positive predictive value). Indeed, it is not only CAARMS criteria that determine the actual risk of psychosis-transition but also the underlying prevalence of psychosis-risk in the population referred. In a recent meta-analysis, psychosis risk in populations seeking help at high risk services was on average 0.15 (at 38 months)². This is significantly higher than the 0.001 risk of psychosis within 38 months (incidence of psychosis 0.0317 per 100 person-years 95%CI: 0.025-0.041)³ in the general population. Specifically, there is meta-analytical evidence that intensive community outreach campaigns promoting referrals to high risk services may actually dilute the risk enrichment of populations undergoing risk (e.g. CAARMS) assessment, resulting in low transitions. Non-specific referrals in Perez’ study¹ could lead to such a dilution of risk enrichment and transitions. We have hypothetically tested this hypothesis. We used the pre-test probability of psychosis estimated in primary care services, reported by the UK Health Improvement Network (THIN) epidemiological primary care database⁴. Based on more than 10 million longitudinal patient records from 437 general practices a rate of first diagnosis of

schizophrenia or non-organic psychoses of 31.3 per 100,000 person years is indicated (corresponding to a 0.00099 risk of psychosis over 38 months)⁴. Using our meta-analytical probability modifying plot (positive likelihood ratio=1.82, negative likelihood ratio=0.09²), we estimated the hypothetical positive and negative post-test probabilities (at 38-month follow-up) associated with a CAARMS assessment in populations referred from UK GP's. The post-test probability for developing psychosis over 38 months was less than 0.001 in case of a negative risk assessment (e.g. CAARMS negative) and only 0.002 in case of a positive risk assessment (e.g. CAARMS positive). This suggests a very limited clinical utility of in-depth risk assessments for psychosis in GP's practices. However, these numbers are only hypothetical and might not hold against real-life numbers that we hope the authors will provide by following-up their sample, thus dismissing our concerns by showing a clinically significant real risk of high transitions in their population.

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